Esophageal Cancer: A Less Common But Deadly Cancer

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Mary McGreal DNP, RN, ANP-C, CCRN, CMC,
Adjunct Professor at Stony Brook University School of Nursing

Objectives

• Discuss the incidence of esophageal cancer?
• Discuss squamous cell cancer and adenocarcinoma of the esophagus?
• Explain the TNM staging classification system?
• Discuss the diagnostic work-up and treatment modalities for esophageal cancer?

Disclosure Statement

• No disclosures
Significance

- Esophageal cancer is a serious malignancy with regards to mortality and prognosis.

Worldwide

- 8th most common malignancy
- 6th most common cause of cancer-related deaths

http://globocan.iarc.fr/

Significance

- Esophageal cancer is not considered a common cancer in the United States
  - 16,910 new cases diagnosed 2016
  - 15,690 deaths
- Despite these facts, it receives little mention when compared with other cancers in terms of health promotion and education.
  - It is 3-4 x more common in men


Significance

- It is 3-4 x more common in men
  - One of the few cancers that is contributing to increasing death rates among males in the United States
  - The long-term prognosis is grim with overall 5 year survival rate of 18.4%
    - Due to its insidious progression most patients diagnosed with advanced disease
    - Survival is dependent on stage

Background

- The esophagus is a hollow muscular tube that connects the throat to the stomach
- It lies behind the trachea and in front of the spine
- Serves as a conduit

Lacks a Serosa Layer
Esophageal Cancer

- Two most common subtypes
  - Squamous cell cancer
  - Adenocarcinoma
- Squamous cell cancer
  - Originates from the cells that line the esophagus
  - It occurs in the upper & middle portion
  - It affects African American males
- Adenocarcinoma
  - Originates from the cells that secrete mucus
  - It occurs in distal esophagus
  - It affects middle aged Caucasian males

Epidemiological Shift

- Epidemiology of esophageal cancer has changed over several decades
- Squamous cell carcinoma was responsible for 90% of the cases of esophageal carcinoma in the United States forty years ago
- Adenocarcinoma is now the leading cause of esophageal cancer in the United States

Risk Factors

- Chronic irritation causes changes in the cells.
- Smoking
- Alcohol
- Achalasia
  - Sphincter fails to relax
- Obesity
  - Risk factor for reflux disease
- Reflux disease
  - Metaplasia \rightarrow\text{ Dysplasia}
  - Risk factor for Barret’s esophagus
Risk Factors

- Barret’s esophagus
  - Squamous epithelium is replaced by intestinal columnar epithelium
  - Esophagus is not equipped to handle ACID
- Age >60
  - Demographic transition
- Male 4 x

Signs & Symptoms

- Dysphagia
  - Most common presenting symptom
  - Solids → Liquids as the tumor progresses
  - Esophageal lumen narrowed >50%
- Hoarseness (laryngeal nerve)
- Pain behind breast bone
- Hiccups
- Vomiting
- Weight loss
Screening

- Screening the general public for is not recommended by any professional organization at this time
- Risks outweigh the benefits
- In lieu of no screening health promotion and education
- In the case of known Barret's disease routine endoscopy is encouraged
- Frequency determined by degree of dysphasia


Diagnosis & Staging

- Barium swallow
  - First test for patient presenting with swallowing issues
- Esophagogastroduodenoscopy
  - EGD allows for direct visualization and biopsies of the tumor
  - Diagnosis is confirmed with a biopsy
- Endoscopic ultrasonography
  - EUS most sensitive test for T and N staging
- Computed tomography (CT) scan of the abdomen and chest
  - Assesses lung, liver metastasis and invasion of adjacent structures
- Positron emission tomography (PET) scan (staging)
- Bronchoscopy
  - To exclude invasion of the trachea or bronchi
- Laparoscopy and thoracoscopy (staging regional nodes)

www.halstedsurgery.org/

Staging Esophageal Cancer

- The TNM (tumor, node, metastasis) system is the most widely used cancer staging system.
- It is based on several key pieces of information:
  - T = depth of the tumor in the wall of the esophagus
  - N = number of lymph node spread
  - M = distant metastases (spread to other parts of the body)
- Once the T, N, and M are determined, an overall stage of 0, I, II, III, IV is assigned. These stages are subdivided, using letters such as IIIA, IIIB.

www.AJCC.org
Esophageal Cancer Staging

Updated in 2010 in 7th ed. of AJCC

- **T status**
  - Tis: Carcinoma in situ/high-grade dysplasia
  - T1: Lamina propria or submucosa
  - T1a: Lamina propria or muscularis mucosa
  - T1b: Submucosa
  - T2: Submucosa or muscularis propria
  - T3: Adventitia
  - T4: Other adjacent structures (pleura, pericardium, or diaphragm)
  - T4a: Other adjacent structures
  - T4b: Other adjacent structures (aorta, trachea)

- **N status**
  - N0: No regional lymph node metastases
  - N1: 1-2 regional lymph nodes
  - N2: 3-6 regional lymph nodes
  - N3: >6 regional lymph nodes

- **M status**
  - M0: No distant metastasis
  - M1: Distant metastasis
    - M1a and M1b are site dependent

- **Grade**
  - G1: Well-differentiated
  - G2: Moderately differentiated
  - G3: Poorly differentiated

Tumor Staging

- Depth of the invasion defines the staging of primary tumor
- Tis (intraepithelial)
  - No invasion of basal membrane
- T1 (beyond the basal membrane)
  - Invade lamina propria, muscularis mucosa or submucosal
    - T1a = Mucosal or T1b = Submucosal
- T2 (breach in to but not beyond muscularis propria)
- T3 (invade beyond the esophageal wall without invading adjacent structures)
- T4
  - T4a, T4b = unresectable

Progressive Invasion of the Tumor

- The detection of the depth of the invasion is crucial for staging
Pattern of Spread

- Prognosis is dependent on local invasion as well as spread to regional and distant structures within the body.
- Direct extension
  - Lack of serosal layer
- Lymphatic spread
  - Lymph node involvement increases with T stage
- Hematogenous spread
  - Mostly seen in advanced cancer

Esophageal Cancer Staging

<table>
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Management

- Tumor stage determines goals of treatment:
  - Cure
  - Prolong survival
  - Palliative cancer related symptoms
- Management depends on:
  - Extent of the disease
  - Co morbidities
  - Patient preference
Endoscopic Therapy

- Endoscopic therapies have become attractive procedures as both diagnostic and therapeutic modalities
  - Endoscopic Mucosal Resection (EMR)
  - Endoscopic Submucosal Dissection (ESD)
- Used in management of tumors < 2 cm
- Used to treat both adenocarcinoma and squamous cell cancer

Endoscopic Therapy

- EMR is popular in United States
- Stage 1
  - Tis and T1aN0
- Able to achieve negative resection of the tumor while avoiding an invasive esophagectomy

Endoscopic Therapy

- Shrinks the tumor locally
- Systemic disease
- Trimodality therapy
- Esophagectomy
- Esophageal cancer
- Surgery
- Radio-therapy
- Chemo-therapy

Trimodality therapy

Endoscopic procedure

Shrinks the tumor locally
Trimodality Therapy

• The aim of neoadjuvant chemoradiation is to reduce the bulk of the primary tumor before surgery to facilitate higher curative resection rates
• Stages II-III
• Neoadjuvant therapy for esophageal cancer is as follows:
  » Combination of radiotherapy and chemotherapy
  » Usually administered over a 45-day period, with esophageal resection after approximately 4 weeks

Trimodality therapy

• Several trials and meta-analyses support the view that a concurrent trimodality therapy provides a survival benefit compared with surgery alone.
• Dutch CROSS trial - 363 patients
  » Median overall survival was 48.6 months in the neoadjuvant group vs 24.0 months in the surgery-alone group
• CALGB 9781 - 56 patients
  » Median survival of 4.48 vs 1.79 years in favor of trimodality therapy
• Meta-analyses – 12 Randomized trials
  » Neoadjuvant chemoradiation versus surgery alone for esophageal or EGJ cancer. The benefit was similar across histologic subtypes.

Results support TRIMODALITY approach

Esophagectomy

• Standard curative treatment for early stage esophageal cancer
• Three approaches
  » Transhiatal esophagectomy (THE)
  » Transthoracic esophagectomy (TTE)
  » Minimally invasive esophagectomy
• Choice of approach dependent on:
  » Stage of cancer
  » Tumor location
Post-Operative Complications

- Cardiac Arrhythmias
  - Atrial fibrillation
  - Due to stimulation of vagal nerve
  - Digoxin or beta blockers

- Pulmonary
  - Atelectasis and pneumonia
  - Ventilated >24 hrs
  - Anastomotic leak (2-10 days post op)
    - Cervical region

Post-Operative Complications

- Chylothorax
  - Nicking of thoracic duct
    - Increased drainage in chest tube
    - Milky white appearance, high fat content, triglyceride is a marker
    - Stop tube feeds or surgical ligation

Nutritional Management

- Gastrostomy tube inserted during surgery to aid with nutrition
- Tube Feeds started as early as POD #4
- Barium swallow
- Sips → advance to solids by time of discharge
Inoperable Esophageal Cancer

- Stage IV and distant metastatic disease
- Palliative approach
- Goals:
  - Increase survival time
  - Pain control
  - Emotional support

Palliative Chemoradiotherapy

- Photodynamic therapy
- Stent
- Chemoradiotherapy
- Gastrostomy Tube

Non-obstructive vs Obstructive Esophageal Cancer

Obstructive Esophageal Cancer
Stent Placement

- Self-expandable metallic stents
- Side effects pain, bleeding, migration of the stent

Photodynamic Therapy (PDT)

- Injected with photosensitizing drug which accumulates in tumor
- Light activates the drug which kills the cancer cells
- Most common side effect is sensitivity to bright light which last 4-6 weeks
- Procedure can be repeated

Conclusion

- Esophageal cancer is a growing health concern that is expected to increase in incidence over the next 10 years.
- It is 3-4 x more common in men.
- 5 year survival rate 18.4%
- It is staged according to the widely accepted TNM system
- Staging plays an integral part in guiding stage specific treatment protocols and has a great impact on overall survival.
- Surgery is the standard of care for early staged esophageal cancer
- Trimodality therapy is the standard option for locally advanced esophageal cancer in surgically eligible patients.
Esophageal Awareness

Thank You

References

- American Joint Committee on Cancer. Cancer staging system. www.AJCC.org